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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	6

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application N .	Applicant(s)	
	10/018,974	HIRATA ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Amendment Entry

1. The preliminary amendment filed December 26, 2001 has been entered. The examiner acknowledges the amendment to the specification. Claims 5, 10, 12 and 13 have been amended. Claims 1-18 are under consideration in this office action.

Specification

2. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a deposit rejection.

The specification and claims lack complete deposit information for the deposit of polyclonal antibody α6715. Because it is not clear that cell lines possessing the properties of polyclonal antibody α6715 are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of polyclonal antibody α6715, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are

required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the polyclonal antibody α6715 described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

4. Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the detection of *S.sobrinus*, a diagnostic method for judging risk and an immunochromatographic strip using polyclonal antibody α6715 wherein in each method or apparatus the test fluid must contain at least a concentration of 10^5 to 10^7 cells/ml of *S.sobrinus* in order to allow the antibody with the binding ability for *S.sobrinus* to be not less than 100 times that for *S. mutans* to detect the *S.sobrinus*, does not reasonably provide enablement for a method for the detection of *S.sobrinus*, a diagnostic method for judging risk and an immunochromatographic strip. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification clearly teaches that there is no detection of a color line and thereby no rating when the concentration of *S.sobrinus* cell/ml is less than 10^5. Thus, if the concentration is below that threshold one cannot determine the degree of risk of the dental caries, see page 44, table 1 and 2. Likewise Table 3 shows similar results when the antibody is immobilized onto a strip, see page 45 table 3. The specification teaches, page 52-54 and within Tables 7 and 8, that when adding less than 5x 10^5 cells/well of *S.sobrinus*, the reactivity of polyclonal antibody α6715 is not less than 100 times the reactivity with *S.mutans*. Therefore, only when the concentration of *S.sobrinus* cells/ml is higher than 10^5 can the antibody detect at not less than 100 times the reactivity with *S.mutans*.

There is no teaching within the specification of any detection of S.sobrinus when the concentration is below 10^5 yet the reactivity of the polyclonal antibody α6715 is not less than 100 times the reactivity with *S.mutans*. The specification fails to teach examples of any other polyclonal antibodies with the binding qualifications that meet the limitations of the claims or can be used in the manner instantly claimed. Therefore, the specification fails to enable a method for the detection of *S.sobrinus*, a diagnostic method for judging risk and an immunochromatographic strip wherein there is no minimum concentration of 10^5 to 10^7 cells/ml of *S.sobrinus* using an antibody with the binding ability for *S.sobrinus* to be not less than 100 times that for *S. mutans* to detect the *S.sobrinus*.

Applicants' have provided no guidance to enable one of ordinary skill in the art as to how determine, without undue experimentation, every antibody that meets the

claimed limitations; therefore, one of skill in the art would have to locate de novo steps required for a method of detection and method for judging risk.

Given the lack of guidance contained in the specification and the unpredictability for determining and diagnosing the presence of *S.sobrinus*, one of skill in the art could not make or use the broadly claimed invention without undue experimentation. The specification fails to provide an enabling disclosure for a method for the detection of *S.sobrinus*, a diagnostic method for judging risk and an immunochromatographic strip, simply comprising a provision step, a contact step and an assaying step, which could meet the limitations of the methods as recited in the claims. There is no requirement or limitation for using polyclonal antibody α6715 wherein in each method or apparatus the test fluid must contain at least a concentration of 10^5 to 10^7 cells/ml of *S.sobrinus* in order to allow the antibody with the binding ability for *S.sobrinus* to be not less than 100 times that for *S. mutans* to detect the *S.sobrinus*. In view of the lack of guidance contained in the specification and the unpredictability for the claimed methods, one skilled in the art could not make or use the broadly claimed invention without undue experimentation.

5. Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The preamble of the claims 1-5 is drawn to a method for the detection of *Streptococcus sobrinus* in a test fluid, however the recited steps within the method

comprise a provision step, a contact step and an assaying step. There is no step which correlates assaying the immune complex to detecting *S.sobrinus*. Therefore, the goal of the preamble is not commensurate with the steps of the method that are drawn to detection.

6. Claims 1-13 are unclear. Claims 1 and 6 recite assaying the immune complex, however it is unclear what assays are being done, what method steps are being performed and how the results are analyzed. "Assaying the immune complex" is a generic term which fails to sufficiently describe what the necessary method steps are. For instance, claim 1 fails to recite how the *S.sobrinus* is detected, i.e., is the antibody also labeled to allow detection. Therefore, the claims are unclear

7. Claims 3, 8, and 18 use the term "the mutual ratio between the binding abilities for the serotype d and g strains is within 2" in claims is a relative term which renders the claim indefinite. It is unclear what is being used to determine the ratio. It is unclear how to define within 2, within 2 what? Is the ratio only for certain circumstances, or only when using a particular test? The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the claims are vague.

8. Claims 4 and 9 are unclear. It is unclear how one has a test fluid that already contains the Streptococcus analytes to be detected at specific concentrations. It appears that one is not testing unknown samples but only samples that contain specified concentrations of Streptococcus, to allow binding that is 100 times preferential for S. sobrinus, however it is unclear. Clarification is requested.

9. Claim 6 recites the phrase "derived from the saliva and/or dental plaque," however it is unclear how to define "derived from". The specification does not teach how to make derivatives from saliva and dental plaques. The derivative language is vague and indefinite because the characteristics needed to determine whether an unknown could be considered a derivative of the saliva or dental plaque are unknown. The specification neither discloses a definition for a derivative, nor does it teach a requisite amount of retained qualities needed or characteristics necessary to determine derivatives of saliva or dental plaques. Therefore the claims are unclear.

The term "judging the degree of risk of dental caries" in the claim is a relative term which renders the claim indefinite. The risk is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what the risk is. Is it the risk of any level of infection or the risk that S.sobrinus is present? It is unclear how to define this claim, thus the metes and bounds of the claims are unclear.

10. Claim 13 is unclear. Claim 6 (a) is drawn to preparation of a test fluid derived from saliva or dental plaque. Then dependant claim 13 is drawn to using untreated saliva. It is unclear how the test fluid is derived from saliva, i.e., treated to create this derivative and then in a dependent claim untreated. Clarification is requested to overcome the rejection.

11. Claims 15-16 are unclear. It is unclear how the sample pad operates. If the sample pad absorbs and holds the test fluid, how does the test fluid later flow to the development membrane? It is unclear what the labeled antibody binds to and what it is labeling? It is unclear what will cause the release of the labeled antibody that is temporarily held on the conjugate pad. It is unclear how the detection antibody will detect *S. sobrinus*, if there is no label present. Therefore it unclear how the immunochromatographic strip will function.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 17-18are rejected under 35 U.S.C. 101 because a polyclonal antibody with the binding ability for *S.sobrinus* to be not less than 100 times that for *S. mutans*

as described by the claims is a product of nature. Antisera containing antibodies can be produced from the S. sobrinus bacteria. The claims do not require that the antibody be isolated. Insertion of the terms "isolated or purified" would obviate this rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-13 and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Babaahmady et al. Babaahmady et al., teach determining the presence of both *S.mutans* and *S.sobrinus* as a strong corollary with early caries lesions (abstract). The authors made polyclonal anti-*S.sobrinus* serotype d antibody. The high titre-polyclonal mouse antibody was used in conjunction with a rabbit anti-mouse IgG FITC labeled conjugate for use in indirect immunofluorescence labeling (page 52). The samples tested w0ere clinical plaque samples obtained from children (page 52). The anti-*S. sobrinus* antisera showed no-cross reactions and reacted only with homologous strains and none of the other 75 strains tested (page 52-53). Table 1 shows using the anti-*S.sobrinus* antibody had no cross reaction with *S.mutans* serotypes c, e, f and h. The authors also performed experiments to establish the sensitivity of the antibodies when pooled together (page 53). *S.mutans* and *S.sobrinus* were identified together in many samples (page 53).

Therefore, Babaahmady et al., teach a method for detecting S.sobrinus comprising providing an antibody, bringing the antibody in contact with the test fluid and assaying the complex, likewise Babaahmady et al., teach judging the degree of infection of dental caries and polyclonal antibody.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer (US Patent 5,569,608) in view of Babaahmady et al. Sommer (US Patent 5,569,608) teaches immunochromatographic strips which are popular since they apply visual detection schemes (col. 1 lines 5-9). The immunoassay involves the application of a liquid test sample suspected of containing an analyte to be detected to an application zone or sample pad of an immunochromatographic test strip (col. 1 lines 10-13). The strip is comprised of a matrix through which the test fluid and analyte are suspended and/or dissolved and then will flow by capillarity from the application zone to a detection zone where a visual signal or absence of such reveals the presence of the analyte (col. 1 lines 14-16). The analyte can be detected by using a specific binding partner that bears detectable label (col. 9 lines 16-19). The prior art teaches the use of gold sols as labels for antibodies that are detectable without a chemical change (col. 1

lines 58-60). There is a first zone or conjugate pad, which contains mobile specific binding partner for the analyte which bears the detectable label and can react with the analyte to form an analyte/labeled binding partner and a second zone or development membrane that contained immobilized substance capable of being bound by the active site of the specific binding partner (col. 2 lines 20-28). Then the developed strip can have its signal determined (col. 2 lines 43-45). See also Figures 1 and 3 for immunochromatographic strips.

However Sommer does not teach the use of a polyclonal anti-*S.sobrinus* serotype d antibody. Babaahmady et al., which has been discussed above, teach the antibody and its use in immunological assays.

Therefore it would have been prima facie obvious at the time of applicants invention to modify the immunochromatographic strip of Sommer to include the polyclonal anti-*S.sobrinus* antibody of Babaahmady et al., since no more than routine skill would have been required to exchange the antibody and use one which preferentially detects *S.sobrinus*. One would have a reasonable expectation of success since one of ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent change. Only the expected labeling effect would have been obtained, since the prior art clearly teaches the detection of *S.sobrinus* and relating it to the determination of the bacteria's presence. Therefore a skilled artisan would have had a reasonable expectation of success in switching the antibodies. The use of alternative and functionally equivalent antibodies would have

been desirable to those of ordinary skill in the art based on the availability and known specificity of the polyclonal antibody.

Prior Art

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Skold et al., (US Patent 5,624,809) teach a device for immunochromatographic analysis. Takei et al., teach latex agglutination test particles comprising antibodies against *S.sobrinus* strain B13 (d).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
April 3, 2003

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